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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,275	03/28/2007	Ryozo Nagai	P30563	2170

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EXAMINER	
PURDY, KYLE A	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
09/02/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/598,275	NAGAI ET AL.	
	Examiner	Art Unit	
	Kyle Purdy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,28,29 and 32-48* is/are pending in the application.

4a) Of the above claim(s) *41-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24, 28, 29 and 32-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the amendments filed on 6/29/2010 wherein claims 24, 28, 29 and 32 have been amended, claims 22, 23, 25-27, 30 and 31 have been cancelled and claims 33-48 are newly added.

Election by Original Presentation

2. Newly submitted claims 41-48 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicant requested to change the statutory scope of their invention from composition to method for the previous action. The two groups are:

I. Claims 24, 28, 29 and 32-40, drawn to a method of treatment for arteriosclerosis, classified in class 514, subclass 560.

II. Claims 41-48, drawn to a composition comprising an effective amount of an acyclic polyprenyl compound, classified in class 514, subclass 560.

3. The inventions are distinct, each from the other because of the following reasons:

4. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the process may be practiced with a materially different product such as radionuclides.

5. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 41-48 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Status of Application

6. Claims 24, 28, 29 and 32-40 are pending, claims 41-48 are withdrawn as being directed to nonelected subject matter and claims 24, 28, 29 and 32-40 are presented for examination on the merits. The following rejections are made.

Response to Applicants' Arguments

7. Applicants arguments filed 6/29/2010 regarding the rejection of claims 22, 23, 25-29, 30 and 31 made by the Examiner under 35 USC 103(a) over Marx et al. (Circ. Res., 2002) in view of Shidoji et al. (WO 01/80854), as evidenced by English equivalent US 2005/0250671 have been fully considered and they are found persuasive. This rejection of claims 22, 23, 25-27, 30 and 31 has been overcome by cancellation. The rejection of claims 28 and 29 has been overcome by amendment.

8. Applicants arguments filed 6/29/2010 regarding the rejection of claims 24, 28 and 29 made by the Examiner under 35 USC 103(a) over Marx et al. (Circ. Res., 2002) in view of Shidoji et al. (WO 01/80854), as evidenced by English equivalent US 2005/0250671 have been fully considered but they are not and the rejections are **MAINTAINED** for the reasons of record in the office action mailed on 3/30/2010.

9. In regards to the 103(a) rejection, Applicant asserts the following:

A) The claims as amended are now distinguished over the art; and

B) Marx and Shidoji do not overlap and one would not envisage their combination.

10. In response to A, the amendments made to the claims do not distinguish Applicants invention from the art. The art suggests that arteriosclerosis may be treated by administering acyclic polyprenyl compounds. While it has not been recognized that administration of acyclic polyprenyl compounds inhibits KLF5, this would have been a necessary result of administering acyclic polyprenyl compounds. Artesians of ordinary skill may not have recognized these properties of the obvious method. However, the discoveries of these properties do not render the obvious method patentably new. Additionally, with respect to the added limitation of vascular remodeling, this is obvious because Marx teaches that PPAR activators (i.e. 3,7,11,15-tetramethyl-2,4,6,10,14 hexadecapentanoic acid) are useful for reducing inflammation in transplant associated arteriosclerosis.

11. In response to B, Marx teaches PPAR activators are useful anti-inflammatory mediators. It's taught that the anti-inflammatory response elicited is useful in treating arteriosclerosis and atherogenesis, as well as transplantation-associated arteriosclerosis. Shidoji teaches that 3,7,11,15-tetramethyl-2,4,6,10,14 hexadecapentanoic acid is a PPAR-activator. Thus, any person would readily envisage using 3,7,11,15-tetramethyl-2,4,6,10,14 hexadecapentanoic acid in the method of Marx with a reasonable expectation for success in reducing inflammation associated with arteriosclerosis, thereby treating said condition.

Maintained Rejections, of Record (claim 24) and New Rejections, Necessitated by Amendment (claims 28, 29 and 32-40)

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. **Claims 24, 28, 29 and 32-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marx et al. (Circ. Res., 2002, 90, 703-170) in view of Shidoji et al. (WO01/80854; published 04/23/2001) as evidenced by the English equivalent, US 2005/0250671.**

16. Marx is directed to PPAR activators as anti-inflammatory mediators in human T lymphocytes. It's taught that activation of T lymphocytes and their ensuing elaboration of proinflammatory cytokines represents a critical step in atherogenesis and arteriosclerosis (see abstract). Marx also teaches that these proinflammatory cytokines are also integral to the development of transplantation-associated arteriosclerosis (Tx-AA) (see abstract). Marx shows that activation of PPAR results in marked reduction in cytokine mRNA expression and thus activation of PPAR limits the expression of proinflammatory cytokines yielding potential therapeutic benefits in pathological process like atherosclerosis and Tx-AA (see abstract). Marx is directed to PPAR activation in humans.

17. Marx fails to teach the administration of a polyprenylcarboxylic acid compound, specifically 3,7,11,15-tetramethyl-2,4,6,10,14 hexadecapentanoic acid (THA), as being a PPAR activator for treatment of arteriosclerosis.

18. Shidoji (the English equivalent) is directed to activators of peroxisome proliferative-activated receptors comprising the polyprenylcarboxylic compound, THA. It's taught that THA effectively activates PPAR (see [0009], Example 2 and [0028]). Shidoji teaches that THA is suitable for oral administration and may be combined with pharmaceutical carriers (additives) such as lactose and glucose (see [0019]). Shidoji teaches that THA is suitable for human consumption (see [0021]).

19. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Marx with Shhidoji with a reasonable expectation for success in arriving at a method of treating arteriosclerosis by administering a polyprenylcarboxylic acid such as THA. Marx teaches that PPAR activation results in significant

reduction in proinflammatory cytokines. Moreover, Tx-AA is characterized by smooth muscle cell proliferation, which is believed to be driven by cytokine and cytokine-induced growth factors. PPAR activation may oppose this response as the anti-inflammatory effects of PPAR activation on T lymphocytes contribute to decreased Tx-AA in patients. Although Marx fails to teach administering THA to elicit a PPAR response and treat arteriosclerosis, any ordinary person would have been capable of arriving at such. Shidoj teaches that THA is an excellent PPAR activator and can be administered orally with other pharmaceutical additives. Thus, an ordinary person would be motivated to select and administer THA on subjects with arteriosclerosis with a reasonable expectation in treating the said condition. With respect to the limitations that administration of the polyprenylcarboxylic acid treating arteriosclerosis such that activation of transcription factor KLF5 and vascular remodeling is inhibited, these are interpreted by the Examiner as inherent properties of administering polyprenylcarboxylic acid to treat arteriosclerosis. In other word, administering a polyprenylcarboxylic acid to a subject to treat arteriosclerosis would necessarily have the biological benefits espoused by Applicant, i.e. inhibition of KLF5 and vascular remodeling. Artisans of ordinary skill may not recognize the inherent characteristics or functions of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. With respect to the limitation that the arteriosclerosis be due to vascular injury, wherein the vascular injury is the result of reconstructive surgery, this limitation is met by Marx because Marx teaches that arteriosclerosis may be associated with transplantation surgery, i.e. reconstructive surgery. Regardless, the means by which arteriosclerosis is formed is immaterial to the claim. Absent

secondary considerations, it's the position of the Examiner that arteriosclerosis is arteriosclerosis, regardless of what caused it. In other words, arteriosclerosis caused by vascular surgery would be expected to be identical to arteriosclerosis not caused by vascular surgery, and therefore treatment with a polyprenylcarboxylic acid would reasonably be expected to treat each. Therefore, a method of administering a polyprenylcarboxylic acid for the treatment of arteriosclerosis is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

21. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

23. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

24. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
August 19, 2010

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611
August 30, 2010